

### **REMARKS**

Claims 1 and 3 have been amended. Claims 9, 11, 13, 23-61, and 62 have been canceled. New claims 63-69 have been added. Support for these new claims can be found in the originally filed claims and throughout the specification. Accordingly no new matter has been added. Currently, claims 1-8, 10, 12, 14-22, 63-69 are pending.

### **INTERVIEW SUMMARY**

Applicants wish to thank the Examiner and his supervisor for attending an in-person interview held June 9, 2009. No demonstration was conducted. A chart of the claim 1 compared to the prior art was discussed during the interview. All of the cited prior art was discussed. Applicants discussed adding in new claims closer to the originally filed claims. The principal thrust of the discussion related to Kirpotin not teaching pegylated liposomes. No agreement was reached.

### **ARGUMENTS**

#### **Claim rejections under 35 USC §112, second paragraph.**

The Examiner has rejected claims 1-8, 10, 12 and 14-22 under 35 U.S.C. §112, second paragraph. Applicants submit that the claim amendments render this ground of rejection moot and request withdrawal of this ground of rejection.

#### **Claim rejections under 35 U.S.C. §103(a).**

Claims 1-8, 10, 12, 14-22, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over the following references in various combinations: Kirpotin (6,110,491) in view of Wong (US 2005/0025822), Mammarella (US 2006/0078605) individually or in combination further with Papahadjopoulos (4,235,871); Hong (Clinical Cancer Research 1999); Janoff (4,880,635); Radhakrishnan (5,192,528) or Uchiyama (International J of Pharm 1995); Forssen (5,714,163)

Applicants disagree and point out that none of the cited references, alone or in combination teach or suggest two of the claim elements: 1) an aqueous hydration buffer comprising ammonium sulfate and sucrose; and 2) removing ammonium sulphate from extraliposomal hydration medium using a sucrose-histidine buffer solution.

**"an aqueous hydration buffer comprising ammonium sulfate and sucrose"**

The claims require an aqueous hydration buffer comprising ammonium sulfate and sucrose. Not one of the references cited by the Examiner teach this element. The Examiner's primary reference, Kirpotin, does not teach an aqueous hydration buffer comprising ammonium sulfate and sucrose. Kirpotin actually teaches away from using ammonium sulfate and sucrose because when Kirpotin used ammonium sulfate alone, his pegylated liposomes had the lowest performance. Kirpotin found that ammonium sulfate gives a poor precipitation and thus poor loading efficiency but found that polyacrylate type precipitating agents in the hydration medium provided a better loading efficiency. One skilled in the art after reading Kirpotin would thus not be motivated to take ammonium sulfate, which did not work well and combine it with sucrose when Kirpotin leads the reader to abandon the use of ammonium sulfate altogether and instead use a polymer such as polyacrylate. Further, Kirpotin is directed to a loading mechanism and this mechanism involves forming a precipitate with a polymer whereas the ammonium sulfate and sucrose solution used in the present invention is for forming the liposomes. There is thus no teaching or suggestion by Kirpotin to use hydration buffer comprising ammonium sulfate and sucrose, let alone combine it with any other reference teaching ammonium sulfate or sucrose.

Wong and Mammarella did not use ammonium sulfate and sucrose and in addition, these references are not proper prior art as they are after the priority date of the present application.

In addition, Papahadjopoulos, Hong, Radhakrishnan, and Uchiyama do not use ammonium sulfate and sucrose in the hydration buffer either.

Further, Forssen does not teach an aqueous hydration buffer comprising ammonium sulfate and sucrose. Forssen has a buffer with ammonium salt or sucrose but does not teach a hydration buffer with ammonium sulfate and sucrose.

Emmanuel also does not teach an aqueous hydration buffer comprising ammonium sulfate and sucrose. Emmanuel's hydration buffer only has ammonium sulfate. Sucrose is used for tonicity in the composition but sucrose and ammonium sulfate are not used as a hydration buffer as required by the claims.

Thus, none of the cited art teaches or suggests the claim element of an aqueous hydration media comprising ammonium sulfate and sucrose. For this reason alone, all of the 35 U.S.C. § 103(a) rejections should be withdrawn. In addition, as shown below, none of the cited references teach

another claim element: “removing extraliposomal hydration media using a sucrose-histidine buffer solution.”

**“removing extraliposomal hydration media using a sucrose-histidine buffer solution”**

The cited references do not teach another claim element – namely removing extraliposomal hydration media using a sucrose-histidine buffer solution.

Neither Kirpotin, Forssen, Janoff, Papahadjopoulos, Hong, Radhakrishnan, Uchiyama, Emmanuel, Mammarella or Wong teach or suggest removing extraliposomal hydration media using a sucrose-histidine buffer solution, as required by the claims. In addition, as mentioned above, Mammarella and Wong are not proper prior art references as they were published after the priority date of the instant application. Although Papahadjopoulos mentions histidine in a hydration buffer, there is not teaching or suggestion to use a sucrose-histidine buffer solution for removing extraliposomal hydration media. Emmanuel mentions histidine for pH control but does not teach or suggest a sucrose-histidine buffer solution for removing extraliposomal hydration media.

Thus, none of the cited art teaches or suggests the claim element of removing extraliposomal hydration media using a sucrose-histidine buffer solution. For this reason alone, all of the 35 U.S.C. § 103(a) rejections should be withdrawn. In addition, as shown above, none of the cited references also teach another claim element of the hydration media comprising ammonium sulfate and sucrose. Therefore there are at least two claim elements not taught or suggested by any of the references alone or in combinations. As such, the 35 U.S.C. § 103(a) rejections are improper and should be withdrawn. Applicants request withdrawal of these grounds of rejection and allowance of the pending claims.

### CONCLUSION

Thus, applicants have shown that none of the cited references actually teach each and every element of the claim nor do they suggest these elements, and the combination of every cited reference does not teach or suggest all of the claim elements. Accordingly, applicants request withdrawal of all of the rejection and request allowance of the present claims. The Commissioner is hereby authorized to charge any fee or credit any overpayment to Deposit Account No: 50-4254.

Respectfully Submitted,

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